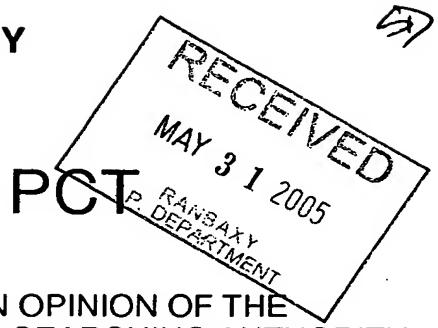


# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220



## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

|  |  |   |
|--|--|---|
|  |  | Date of mailing<br>(day/month/year) see form PCT/ISA/210 (second sheet) |
| Applicant's or agent's file reference<br>see form PCT/ISA/220  |  | <b>FOR FURTHER ACTION</b><br>See paragraph 2 below                      |
| International application No.<br>PCT/B2004/003571  | International filing date (day/month/year)<br>01.11.2004 | Priority date (day/month/year)<br>07.11.2003                            |
| International Patent Classification (IPC) or both national classification and IPC<br>C07D501/00, A61P31/00, A61K31/545 |  |   |
| Applicant<br>RANBAXY LABORATORIES LIMITED  |  |   |

### 1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

|   |   |
|---|---|
| Name and mailing address of the ISA:  | Authorized Officer                          |
| <br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 eprmu d<br>Fax: +49 89 2399 - 4465 | Schmid, A<br>Telephone No. +49 89 2399-8591 |
|    |   |

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITYInternational application No.  
PCT/IB2004/003571

IAP20 Rec'd PCT/PI 05 MAY 2006

**Box No. IV Lack of unity of invention**

1.  In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
  - paid additional fees.
  - paid additional fees under protest.
  - not paid additional fees.
2.  This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
  - complied with
  - not complied with for the following reasons:  
**see separate sheet**
4. Consequently, this report has been established in respect of the following parts of the international application:
  - all parts.
  - the parts relating to claims Nos.

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. Statement

|                     |             |                        |
|---------------------|-------------|------------------------|
| Novelty (N)         | Yes: Claims | 14,17,18-24,36-44      |
|                     | No: Claims  | 1-13,15,16,25-35,45,46 |
| Inventive step (IS) | Yes: Claims |                        |
|                     | No: Claims  | 14,17-24,36-44         |

|                               |             |      |
|-------------------------------|-------------|------|
| Industrial applicability (IA) | Yes: Claims | 1-44 |
|                               | No: Claims  |      |

## 2. Citations and explanations

**see separate sheet**

**Re Item IV**

**Lack of unity of invention**

- 1) The examiner agrees with the opinion of the search report. The applicant's attention is drawn to the reasoning as indicated there.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**Invention 1 according to the search report:**

- 1) The applicant has claimed in present claims 1-5 a cefditoren pivoxil characterised by a certain purity. However, the applicant's attention is drawn to the fact that the purity of a compound could **never** render that compound novel.

Accordingly all documents which disclose either crystalline or amorphous cefditoren pivoxil are novelty destroying for present claims 1-5.

Therefore, the applicant's attention is drawn to

D1: US-B1-6 342 493 (ONODERA MASAHIRO ET AL) 29 January 2002 (2002-01-29)  
D2: US-B1-6 294 669 (YASUI KIYOSHI ET AL) 25 September 2001 (2001-09-25)

which both disclose in their examples crystalline or amorphous cefditoren pivoxil.

Therefore the subject-matter of present claims 1-5, 45 and 46 is not novel with regard to Article 33(2) PCT.

not to be novel since all process steps are either explicitly known from D5 (resulting in the same purity) or within the general knowledge of a skilled person.

4) Merely the use of a second solvent in order to precipitate the cefditoren pivoxil as disclosed in present claims 18-24 is not explicitly described in D5. However, in view of the fact that the general principle of precipitation is known from D5 and that such a measure (choice of a solvent the compound is not soluble in) constitutes general knowledge for a skilled person the subject-matter of present claims 18-24 does in no way involve any inventive step with regard to Article 33(3) PCT.

**Invention 3 according to the search report:**

1) The subject-matter of present claims 36-43 differs from the prior art represented by

D6: EP-A-1 051 978 (MEIJI SEIKA KAISHA, LTD) 15 November 2000 (2000-11-15) and

D7: US 2002/037322 A1 (ONODERA MASAHIRO ET AL) 28 March 2002 (2002-03-28)

in that the acid solution is neutralised with a sodium hydroxide solution thus effecting precipitation (cf. D6 and D7, examples) instead of using water for the same purpose. Also the degree of purity of the amorphous cefditoren pivoxil is not explicitly indicated.

Accordingly the subject-matter of present claims 36-43 is novel pursuant to Article 33(2) PCT.

However, looking at D6 and D7 it becomes evident that the way of precipitation is simply quicker in D6 and D7 since the pH-value changes more rapidly. A skilled person starting from D6 or D7 looking for an alternative way of obtaining a very pure amorphous cefditoren pivoxil would simply try to modify and refine the known process which can be easily done by a few routine experiments. If there is no interest in the additive which is present in D6 and D7 (cf. cellulose derivative), one

would simply leave it out.

Therefore, the subject-matter of present claims 36-43 does not involve an inventive step with respect to Article 33(3) PCT.

**Invention 4 according to the search report:**

- 1) Present claim 44 simply discloses the conversion of a mixture of the amorphous and crystalline mixture of cefditoren pivoxil into pure amorphous cefditoren pivoxil without indicating any process steps.

Since a **mixture** of the amorphous and crystalline cefditoren pivoxil as initial product in order to obtain pure amorphous cefditoren pivoxil is not explicitly known from the prior art the subject-matter of present claim 44 is formally novel pursuant to Article 33(2) PCT.

- 2) However, since no reaction steps are indicated, this process cannot be carried out and no inventive step can be acknowledged since a skilled person could easily use the processes as indicated in D5 to D7 in order to obtain the pure amorphous cefditoren pivoxil as indicated in present claim 44.

Therefore the subject-matter of present claim 44 does not involve an inventive step with regard to Article 33(3) PCT.